ing of the peak relative to an arbitrary time origin) are then measured from the fitted curve. The pattern of blood pressure is not symmetrical within a 24 hour cycle; for example, a single cosine function would be a very poor fit to the systolic data in Fig. 1 of our paper. This observation appears to be confirmed by the work of Murnaghan *et al* in their study of blood pressure in pregnancy.[2] The single cosinor technique failed to give sufficient resolution to describe other than gross features of the blood pressure patterns. Walsh and Goldberg also found that significant components were present at higher frequencies.[3] Detailed studies by Sayers[4] indicate the presence of several concurrent patterns, posing severe problems in any detailed statistical analysis across patients. More recently, the same group has suggested a set of procedures for pattern analysis of these records, relying more on measurements from each record than on a priori models.[5] These procedures are at present being applied to blood pressure data from a variety of sources.

In active untreated subjects the timing of the acrophase must be heavily dependent on the time of waking since this is the event which has the greatest effect on blood pressure. This would tend to place the acrophase at approximately 14 hours before waking—that is, at 1800 or so, and this has been the finding of several workers.[3 6] It is hard to see how this would provide any illumination of our observed shifts in the nadir of blood pressure at around 0100–0300. For critical studies we now compile our data relative to waking time as well as to absolute clock time.

We are therefore unconvinced that cosinor analysis would clarify our observations of ambulatory intra-arterial blood pressure unless applied in a complex form taking account of many pattern features and frequencies, in which case conventional Fourier analysis seems to offer more possibilities.

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# Delayed recovery of left ventricular function after antithyroid treatment

Sir,

Forfar *et al* (1984; 52: 215–22) suggest that in hyperthyroidism left ventricular function is reversibly depressed. Their conclusions are based on haemodynamic measurements performed on 15 hyperthyroid subjects before and during isometric exercise, and those measurements were repeated after the subjects had been rendered euthyroid. The authors stress that hyperthyroidism involves changes intrinsic not only to the heart itself but also to the peripheral circulation. They assume, however, that the performance of a standardised isometric exercise task produced the same changes in the peripheral circulation in both hyperthyroid and euthyroid states and, therefore, that exercise caused the same changes in cardiac loading before and after the subjects had been treated for their thyrotoxicosis. Nevertheless, as shown in the Table below, using data taken from their own paper it may be calculated that isometric exercise actually caused directionally opposite changes in peripheral vascular resistance during the thyrotoxic and euthyroid states. Peripheral vascular resistance is a major determinant of the impedance offered to the outflow of blood from the left ventricle. In the study of Forfar *et al* the thyrotoxic heart, faced with an increased peripheral resistance during isometric exercise, did not function as well as it did at rest. In contrast, the euthyroid heart experienced a large reduction in calculated peripheral vascular resistance during isometric exercise and showed no deterioration in function.

Thus it would appear that peripheral resistance is

an important determinant of basal and exercise induced left ventricular function in thyrotoxicosis, and the results obtained by Forfar *et al* do not establish the presence of an intrinsic myocardial abnormality in the thyrotoxic state.

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This letter was shown to the authors, who reply as follows:

Sir,

Northover *et al* do not indicate how they have determined systolic and diastolic volumes from the left ventricular diameters given in our paper. Their derived stroke volume in the euthyroid state at rest, for example (19·4 ml) at a measured heart rate of 82 beats/min, gives a cardiac output of 1·6 l approximately, an output so low that it is biological nonsense in the context of our study. Similarly, their derived figure for cardiac output in the hyperthyroid group at rest (2·8 l/min) is over four times less than that of Merillon *et al*[1] based on direct invasive measurements (13·1 l/min). We doubt whether the errors and assumptions involved in the derivation of left ventricular volumes by single element echocardiography[2] justify their usage in a study of this type, let alone as a basis for calculating peripheral vascular resistance.

The conclusion of our study that left ventricular function is depressed in hyperthyroidism is not dependent on isometric exercise causing the same changes in peripheral vascular resistance in the hyperthyroid and euthyroid state. Indeed, this is most unlikely in view of the profound reduction in peripheral vascular resistance in hyperthyroidism. During isometric exercise vascular resistance will certainly be lower in hyperthyroidism. Crude derivation of vascular resistance from our study (using the formula of Feigenbaum *et al* for ventricular volumes[3]) supports this contention. Despite this reduction in peripheral vascular resistance, the pre-ejection period during isometric exercise was significantly longer in the hyperthyroid (144(4) ms) than in the euthyroid (135(4) ms) state. This significant prolongation in exercise pre-ejection period in hyperthyroidism was maintained after autonomic blockade.

The results of our study suggest reversible abnormalities in left ventricular contractile responses to exercise in hyperthyroidism that may persist for some weeks after the restoration of a biochemical euthyroid state.

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Table *Effects of antithyroid treatment on left ventricular function*

| *Measurement* | *Source* | *Hyperthyroid* | | *Euthyroid* | |
|---|---|---|---|---|---|
| | | *Resting* | *Exercising* | *Resting* | *Exercising* |
| Systolic arterial pressure (mm Hg) | Forfar *et al* | 126 | 151 | 119 | 144 |
| Heart rate (beats/min) | Forfar *et al* | 99 | 108 | 82 | 93 |
| Ventricular diastolic diameter (cm) | Forfar *et al* | 4·2 | 4·3 | 4·0 | 4·1 |
| Ventricular diastolic volume (ml)* | Calculated | 38·8 | 41·6 | 33·5 | 36·1 |
| Ventricular systolic diameter (cm) | Forfar *et al* | 2·7 | 3·2 | 3·0 | 2·9 |
| Ventricular systolic volume (ml)* | Calculated | 10·3 | 17·2 | 14·1 | 12·8 |
| Ventricular stroke volume (ml)* | Calculated | 28·5 | 24·4 | 19·4 | 23·3 |
| Cardiac output (l/min) | Calculated | 2·84 | 2·64 | 1·59 | 2·17 |
| Peripheral vascular resistance (mm Hg min/l$^{-1}$) | Calculated | 44·3 | 57·2 | 74·8 | 66·4 |

*In the calculations of ventricular volume the ventricle was assumed to be spherical.